Ado-trastuzumab emtansine (Kadcyla®)

Criteria for Use

December 2014

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. **THE CLINICIAN SHOULD UTILIZE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.**

The Product Information should be consulted for detailed prescribing information.

See the VA National PBM-MAP-VPE Monograph on this drug at www.pbm.va.gov or http://vaww.pbm.va.gov for further information.

Exclusion Criteria *If the answer to ANY item below is met, then the patient should NOT receive ado-trastuzumab emtansine.*

☐ Unwilling to transfer oncology care to VA provider

☐ History of non-compliance with follow-up appointments or laboratory visits

☐ Known hypersensitivity to ado-trastuzumab emtansine or any of its excipients (sodium succinate, sucrose, polysorbate 20)

☐ Clinically significant cardiovascular disease defined as:

- Baseline Left Ventricular Ejection Fraction (LVEF) < 50% via MUGA or echocardiography
- Uncontrolled hypertension or arrhythmia
- Myocardial infarction within prior 6 months
- CHF (NYHA Class 3 or 4)
- Cumulative prior anthracycline exposure > 360 mg/m^2 of doxorubicin or its equivalent

☐ Breast tissue does not overexpress HER2 protein (HER2 positive status defined as IHC 3+ or FISH amplification ratio $\geq$ 2.0)

☐ Eastern Cooperative Oncology Group (ECOG) Performance Status greater than or equal to 2*

☐ Platelet count < 100,000/ mm^3

☐ Grade 3 or higher peripheral neuropathy

☐ Serum transaminases (ALT/AST) > 2.5x ULN and/or Total bilirubin > 1.5x ULN or active hepatitis B or C virus

☐ Pregnancy

Inclusion Criteria *The answers to the following must be fulfilled in order to meet criteria.*

☐ **Metastatic Breast Cancer Setting**. Diagnosis of metastatic breast cancer and has received prior treatment for metastatic disease that includes trastuzumab and a taxane, separately or in combination.

Patients should have received prior therapy for metastatic breast cancer OR

Developed disease recurrence during or within six months of completing adjuvant therapy

☐ Goals of care and role of Palliative Care consult have been discussed and documented.

For women of childbearing potential

□ Pregnancy must be excluded prior to receiving ado-trastuzumab emtansine and patient provided contraceptive counseling on potential risk vs. benefit of taking ado-trastuzumab emtansine if patient were to become pregnant

Dosage and Administration (refer to prescribing information for dose modifications)

- Ado-trastuzumab emtansine dose is 3.6 mg/kg given as an intravenous (IV) infusion every 3 weeks (21-day cycle) until progressive disease or unacceptable toxicity.
- Do not administer ado-trastuzumab emtansine at doses greater than 3.6 mg/kg.
- Closely monitor infusion site for possible subcutaneous infiltration during administration
- Administer FIRST infusion over 90 minutes. Observe patients during infusion and for at least 90 minutes after for fever, chills or other infusion-related reactions
- Administer SUBSEQUENT infusions over 30 minutes if prior infusions were well tolerated. Observe patient during

infusion and for at least 30 minutes after infusion.

- Do NOT substitute ado-trastuzumab emtansine for trastuzumab!
- Refer to PI for dose modification guidelines for the following:
    - Increased AST/ALT, hyperbilirubinemia
    - Left ventricular dysfunction
    - Thrombocytopenia
    - Pulmonary toxicity
    - Peripheral neuropathy

Monitoring

- LVEF at baseline and every 3 months
- Observe patients for infusion-related reactions for at least 90 minutes following the first infusion and at least 30 minutes following subsequent infusions
- Monitor infusion site for possible infiltration into subcutaneous tissues
- Observe patients closely for possible hypersensitivity reactions.
- Monitor LFT's at baseline and prior to each dose
- Pulmonary toxicity. Patients with baseline dyspnea due to malignancy or comorbidities may be at risk of pulmonary toxicity. Signs/symptoms may include dyspnea, cough, fatigue and pulmonary infiltrates.
- Risk of bleeding. Concomitant thrombocytopenia, anticoagulant or antiplatelet therapy may increase this risk. Use caution and consider more intensive monitoring.
- Platelet count at baseline and prior to each dose. The incidence/severity was shown to be higher among the Asian population. Refer to PI for dose-modifying instructions with thrombocytopenia.
- Monitor patients for signs/symptoms of neurotoxicity. Temporarily discontinue therapy if Grade 3 or 4 peripheral neuropathy occurs.
- Pregnancy test prior to initiation of therapy (if child-bearing potential) and as clinically indicated.

Issues for Consideration

- There is no prospective data to guide the duration of HER2-directed therapy in MBC. Use of ado-trastuzumab emtansine beyond the second-line setting in MBC has been shown to provide a benefit in PFS (TH3RESA); improvement in OS has not been demonstrated. Patients should be aware of risks (toxicity, inconvenience, cost) vs. benefits (improved PFS) when considering ongoing HER2-directed therapy.

Discontinuation Criteria

- Monitor for evidence disease progression in the form of radiographic progression, clinical deterioration and/or serum tumor markers (i.e. CA 15-3, CA 27.29, CEA, circulating tumor cells)

* http://www.ecog.org/general/perf_stat.html

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